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ART UNIT	PAPER NUMBER
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MORRISON & FOERSTER
755 PAGE MILL ROAD
PALO ALTO CA 94304-1018

DATE MAILED: 10/02/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 6/28/96 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), - days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1-5, 22-23, 34-35 are pending in the application.
   Of the above, claims 22-23 (species - agents that are antibodies) are withdrawn from consideration.
2. ☒ Claims 6-21, 24-33 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☐ Claims 1-5, 22-23 are rejected.
5. ☒ Claims 34-35 are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

Part III DETAILED ACTION

Response to Amendment

1. The amendment filed 06/28/96 has been entered.

2. Claims 22-23 (species directed to agents that are antibodies) are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 8. The species election of claims 22-23 is thus the dominant inhibitory fragment of CD40bp. It is noted that the other nonelected claims 6-21 & 24-33 have been cancelled in paper #8.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The Declaration under 37 C.F.R. § 1.132 filed 6/28/96 is sufficient to overcome the rejection of claims 1-5 & 22 based upon being anticipated by Hu et al., as applied under 35 U.S.C. § 102(a). The Declarant states that in Hu et al., co-authors Hong Ming Hu, Karen O'Rourke and Mark S. Boguski worked under the direction of the inventor, Dixit, but made no inventive contribution to the subject matter of the application.

5. The Declaration filed on 6/28/96 under 37 C.F.R. § 1.131 is sufficient to overcome the Sato et al., Mosialos et al. and Cheng et al. references. The Declaration establishes actual reduction to practice in the United States prior to the publication date of Sato et al., Mosialos et al. or Cheng et al.

6. The 35 U.S.C. § 102(a) rejections of claims 1-5, 22-23 are withdrawn due the above Declarations.

7. The 35 U.S.C. § 112, 2nd paragraph rejections of claims 1-5, 22-23 is withdrawn due to the amendment of the claims.

8. Applicant's arguments filed 06/28/96 as paper # 8 have been fully considered but they are not deemed to be persuasive.

9. Claims 1-2 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time of the application was filed, had possession of the claimed invention. The added material which is not supported by the original disclosure is as follows:

a) "and does not specifically bind to a homologous cell-surface receptor of the tumor necrosis receptor family" in

claim 1. No antecedent basis for this recitation can be found in the specification, for example, including pages 1 and 38 of the specification, as stated on page 3 of the response. It is not apparent that the invention as disclosed was contemplated to include the limitation of excluding ligands to the tumor necrosis family.

b) "comprising the C-terminal half" in claim 2. The only recitation apparently is on page 37 in which it is stated that "it appears likely that the C-terminal portion mediates CD40 binding", which appears to be based on the single species example that the C-terminal half that begins at Phe ^{297} on page 37 mediates binding. It is not apparent that the invention as disclosed was contemplated to include the general recitation of "C-terminal half".

Applicant is required to cancel the new matter in the response to this Office action.

10. Claims 1-5, 22-23 are again rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to the human CD40 binding protein of SEQ ID NO 2, for the reasons made of record, and as follows.

Claims 1-3 are rejected as being not commensurate in scope with the specification because the claims as currently recited still encompass any mammalian protein that specifically binds to

any cytoplasmic region of any mammalian CD40 receptor, as well as any CD40bp fragment, without setting forth any physical characterization and little functional characteristics. Although the Applicant argues on page 6 that CD40bp interacted with native CD40 only, this is not what is claimed. The claims still encompass proteins that fulfill the functional language of the claim, but which structurally are different protein molecules with no structural relationship to the disclosed human CD40 ligand. These different protein molecules are not taught within the specification. By contrast, the specification provides guidance for only human CD40bp with the specific amino acid sequence depicted in SEQ ID NO 2. In addition, all fragments from all (64 kD) mammalian proteins having the recited functional language are claimed which have no structural similarity with the enabled protein of SEQ ID NO 2. No fragments except the single C-terminal fragment from amino acid residues 297-567 has been disclosed that has the desired properties of the instant invention. It is thus not predictive based solely from the single enabled human protein of SEQ ID NO 2 that the skilled artisan would be able to make other mammalian proteins. The name "mammalian protein", or a "polypeptide fragment", does not serve to sufficiently characterize and enable the different proteins that are encompassed by the claims. Neither does a "human

protein having a molecular weight of about 64 kD", as discussed in the previous Office action.

With respect to the Applicant's arguments on page 6 of the response that the C-terminus is required for binding to CD40, and that the Applicant has provided in one embodiment the full amino acid sequence for CD40, truncating the amino acid sequence by one or more amino acids in order to make C-terminal polypeptide fragments is not commensurate in scope with the specification, because those residues that are critical for CD40bp's function are not disclosed, nor which residues can be altered and still maintain the desired functional activity of CD40bp. The fact that other investigators have made other polypeptide fragments that fall within the scope of the claims is not the issue. The specification lacks definition on what distinguishes the desired invention from the other structurally unrelated polypeptides and polypeptide fragments claimed, as well as to the minimal length or what amino acid residues are necessary for CD40bp's specific functional activity. Because of this lack of guidance, the skilled artisan is not able to successfully determine without undue experimentation what alterations/truncations are tolerable in order to retain a functional invention, except for the one disclosed functional embodiment of CD40 (i.e., as recited in claim 35).

The Applicant argues that with respect to the term "mammalian", one skilled in the art need not teach, and preferably omits, what is well known in the art, and cites *Hybritech v. Monoclonal Antibodies, Inc.* However, the issue is not the mere recitation of "mammalian", nor that mammalian cells contain a ligand to CD40, but that "different mammalian polypeptides" with no structural similarity to the disclosed human CD40 ligand (CD40bp) are claimed, and that these different polypeptides are not known to one skilled in the art. The Applicant further argues that it would not require undue experimentation for one of ordinary skill in the art to isolate, clone and sequence the homologous intracellular protein in another mammalian species. However, there is insufficient guidance to acheive this invention, because the specification does not teach whether this protein is conserved among different species.

The Applicant argues with respect to claims 22-23 that it is not undue experimentation to screen antibodies, and then references *In re Wands*. However, the antibody species election was not elected (i.e., Group I versus Group III was elected). Since this argument is to a nonelected species (i.e., agents that are antibodies), this argument is moot.

The arguments toward enablement issues surrounding any random fragment as a "dominant inhibitory fragment"/agent are as

discussed above and in the previous Office action. No inhibitory fragment of CD40bp/agent is disclosed in the specification. It is unknown what constitutes a dominant inhibitory fragment of CD40bp (as it relates to claims 22-23), since the specification provides no guidance to what parameters are required for possessing the properties of a dominant inhibitory fragment of CD40bp. For example, it is unknown and not disclosed whether the C-terminal fragment of amino acid residues 297-567 of CD40bp is an inhibitory agent, or not. Nor is it disclosed what amino acid residues are required to generate an inhibitory fragment/ agent. Since no guidance is provided in the specification on how to isolate those fragments that would be predicted by the skilled artisan to still possess the desired "dominant inhibitory" properties of CD40-specific molecules, if any exist, it would require undue experimentation to determine such, for the reasons discussed above and in the previous Office action.

It is suggested that amending these claims to reflect the specific amino acid molecule of SEQ. ID NO 2 should obviate the above rejections.

Allowable Subject Matter

11. Claims 34-35 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in

independent form, including all of the limitations of the base claim and any intervening claims, and provided that no new matter is introduced.

12. It is believed that all pertinent arguments have been answered.

Conclusion

13. Applicant's amendment necessitated the new grounds of rejection/objection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be reached on (703) 308-2957. The fax phone number for this Group is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

STEPHEN G. WALSH
PRIMARY EXAMINER
GROUP 1800

Robert C. Hayes, Ph.D.
September 19, 1996